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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,702	07/31/2001	Nissim Benvenisty	1822/113	3581

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EXAMINER
CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/918,702	BENVENISTY, NISSIM	
	Examin r	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears n the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 18-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-17* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *July 31, 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election of group II, claims 8-17, in Paper No. 9, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 contains the limitation "human embryonic stem cells."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, in step (a) states "embryonic stem cells" which is broader than the preamble which states "human embryonic stem cells." Also in claim 1, step (c), it is confusing as to whether the cells of step (a) are being differentiated or the cells of step (b). If the cells are those of step (a), then the claims is further confusing as to the role of step (b) in the process. Applicant may want to consider changing in step (c) "human embryonic stem cells" to "embryonic cells" as those are the cells isolated from the embryoid bodies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-10 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller (1995) Current Opinion in Cell Biology 7, 862-869 in view of Thomson et al (1998) Science 282, pp. 1145-1147.

Keller teaches the production of embryoid bodies by culturing ES cells in the absence of feeder cells or LIF, and to culture them in liquid media or methyl cellulose containing media on bacterial Petri dishes (page 862, col. 2, lines 5-10). The ES cells grown in these conditions will not adhere to the surface of the culture dish, that the ES cells are grown in suspension, and subsequently form EB's (page 862, col. 2, lines 10-13). In some protocols the EB's are dissociated to form a monolayer and grown on stromal cells to develop into hematopoietic lineage cells (page 863, figure 1(b)). This co-culture provides at least one exogenous factor. Keller teaches that embryoid bodies, when cultured for extended periods of time can generate cells of the hematopoietic, endothelial, muscle and neuronal lineages (page 863, col. 1, lines 5-9). The formation of specific lineages is the formation of specific cell types.

Thomson teaches the production of human embryonic stem cells line, H9 (page 1145, col. 2, parag. 1, line 6-11; and page 1145, col. 2, parag. 1, line 22 to col. 3, line 5). Thomson offers motivation in stating that human ES cells will provide for human transplantation therapies, and that while substantial advances need to be made in the directed differentiation of human ES cells, progress in the directed differentiation of mouse ES cells to neurons, hematopoietic cells and cardiomyocytes has been made (page 1146-1147, bridg. parag.). Motivation comes from Keller teaching that embryoid bodies provide

an approach for defining the earliest steps of commitment from respective precursor population (pages 866-867, bridg. sentence).

Therefore the ordinary artisan at the time of the instant invention would have been motivated to form EB's as taught by Keller using the human ES cells taught by Thomson to determine the genes and functions involved in lineage commitment in early human embryo development.

Claims 8, 11, 13, 15 and 16 rejected under 35 U.S.C. 103(a) as being unpatentable over Keller (1995) Current Opinion in Cell Biology 7, 862-869 and Wobus et al (1987) Cell Diff. 20 (Suppl), 81S in view of Thomson et al (1998) Science 282, pp. 1145-1147.

Keller teaches the production of embryoid bodies by culturing ES cells in the absence of feeder cells or LIF, and to culture them in liquid media or methyl cellulose containing media on bacterial Petri dishes (page 862, col. 2, lines 5-10). The ES cells grown in these conditions will not adhere to the surface of the culture dish, that the ES cells are grown in suspension, and subsequently form EB's (page 862, col. 2, lines 10-13). In some protocols the EB's are dissociated to form a monolayer and grown on stromal cells to develop into hematopoietic lineage cells (page 863, figure 1(b)). This co-culture provides at least one exogenous factor. Keller teaches that embryoid bodies, when cultured for extended periods of time can generate cells of the hematopoietic, endothelial, muscle and neuronal lineages (page 863, col. 1, lines 5-9). The formation of specific lineages is the formation of specific cell types.

Thomson teaches the production of human embryonic stem cells line, H9 (page 1145, col. 2, parag. 1, line 6-11; and page 1145, col. 2, parag. 1, line 22 to col. 3, line 5).

Wobus teaches that the nerve growth factor cause the differentiation of ES cells in vitro to in to neuron-like cells, and enhanced nerve cell differentiation capacity (lines 12-17).

Thomson offers motivation in stating that human ES cells will provide for human transplantation therapies, and that while substantial advances need to be made in the directed differentiation of human ES cells, progress in the directed differentiation of mouse ES cells to neurons, hematopoietic cells and cardiomyocytes has been made (page 1146-1147, bridg. parag.). Motivation comes from Keller teaching that embryoid bodies provide an approach for defining the earliest steps of commitment from respective precursor population (pages 866-867, bridg. sentence).

Therefore the ordinary artisan at the time of the instant invention would have been motivated to form EB's as taught by Keller using the human ES cells taught by Thomson and to culture the ES cells made by disaggregating the EB's to determine the effects of NGF on lineage commitment in early human embryo development.

Claims 8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller (1995) Current Opinion in Cell Biology 7, 862-869 in view of Thomson et al (1998) Science 282, pp. 1145-1147 and Vittet et al. (1996) Blood 88, 3424-3431.

Keller teaches the production of embryoid bodies by culturing ES cells in the absence of feeder cells or LIF, and to culture them in liquid media or methyl cellulose containing media on bacterial Petri dishes (page 862, col. 2, lines 5-10). The ES cells grown in these conditions will not adhere to the surface of the culture dish, that the ES cells are grown in suspension, and subsequently form EB's (page 862, col. 2, lines 10-13). In some protocols the EB's are dissociated to form a monolayer and grown on stromal cells to develop into hematopoietic lineage cells (page 863, figure 1(b)). This co-culture provides at least one

exogenous factor. Keller teaches that embryoid bodies, when cultured for extended periods of time can generate cells of the hematopoietic, endothelial, muscle and neuronal lineages (page 863, col. 1, lines 5-9). The formation of specific lineages is the formation of specific cell types.

Thomson teaches the production of human embryonic stem cells line, H9 (page 1145, col. 2, parag. 1, line 6-11; and page 1145, col. 2, parag. 1, line 22 to col. 3, line 5).

Thomson offers motivation in stating that human ES cells will provide for human transplantation therapies, and that while substantial advances need to be made in the directed differentiation of human ES cells, progress in the directed differentiation of mouse ES cells to neurons, hematopoietic cells and cardiomyocytes has been made (page 1146-1147, bridg. parag.). Motivation comes from Keller teaching that embryoid bodies provide an approach for defining the earliest steps of commitment from respective precursor population (pages 866-867, bridg. sentence).

Vittet teaches the differentiation in vitro of ES cells into endothelial cells by incubation in the presence of IL-6 and other growth factors (page 3427, col. 1, parag.1, lines 2-6 and 3428, col. 1, parag. 1, lines 1-4).

Therefore the ordinary artisan at the time of the instant invention would have been motivated to form EB's as taught by Keller using the human ES cells taught by Thomson and to differentiated the ES cells by growth in the presence of growth factors including IL-6 to determine the genes and process of vascular smooth muscle cell lineage commitment in early human embryo development.

Claims 8 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller (1995) Current Opinion in Cell Biology 7, 862-869 in view of Thomson et al (1998) Science 282, pp. 1145-1147 and Drab (1997) FASEB Journal 11, 905-915.

Keller teaches the production of embryoid bodies by culturing ES cells in the absence of feeder cells or LIF, and to culture them in liquid media or methyl cellulose containing media on bacterial Petri dishes (page 862, col. 2, lines 5-10). The ES cells grown in these conditions will not adhere to the surface of the culture dish, that the ES cells are grown in suspension, and subsequently form EB's (page 862, col. 2, lines 10-13). In some protocols the EB's are dissociated to form a monolayer and grown on stromal cells to develop into hematopoietic lineage cells (page 863, figure 1(b)). This co-culture provides at least one exogenous factor. Keller teaches that embryoid bodies, when cultured for extended periods of time can generate cells of the hematopoietic, endothelial, muscle and neuronal lineages (page 863, col. 1, lines 5-9). The formation of specific lineages is the formation of specific cell types.

Drab teaches the differentiation of ES cells into vascular smooth muscle cells by incubation in the presence of retenoic acid and dibutyryl-cAMP (page 913, col. 1, parag. 1, lines 1-3)

Thomson teaches the production of human embryonic stem cells line, H9 (page 1145, col. 2, parag. 1, line 6-11; and page 1145, col. 2, parag. 1, line 22 to col. 3, line 5).

Thomson offers motivation in stating that human ES cells will provide for human transplantation therapies, and that while substantial advances need to be made in the directed differentiation of human ES cells, progress in the directed differentiation of mouse ES cells to neurons, hematopoietic cells and cardiomyocytes has been made (page 1146-1147, bridg. parag.). Motivation comes from Keller teaching that embryoid bodies provide an approach for defining the earliest steps of commitment from respective precursor population (pages 866-867, bridg. sentence).

Therefore the ordinary artisan at the time of the instant invention would have been motivated to form EB's as taught by Keller using the human ES cells taught by Thomson and to differentiated the ES cells by growth in the presence of retenoic acid and dibutyryl cAMP to determine the genes and process of vascular smooth muscle cell lineage commitment in early human embryo development.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
January 25, 2003